IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTY.'S DOCKET: KORSGREN=1

In re Application of:	)	Confirmation No.: 9165
	)	
Olie KORSGREN et al	)	Art Unit: 1614
	)	
I.A. Filing Date: 02/04/2000	)	Examiner: Donna A. Jagoe
371(c) Date: November 7, 2001	)	
	)	July 30, 2007
U.S. Appln. No.: 09/890,936	)	**MONDAY**
	)	
For: NOVEL USE WITHIN TRANSPLANTATION SURGERY	)	

STATEMENT OF SUBSTANCE OF INTERVIEW

Customer Service Window, Mail Stop Amendment
Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Randolph Building, 401 Dulany Street
Alexandria, Virginia 22314

Sir:

As the last paragraph of the "Interview Summary" of the interview of June 28, 2007, requires a statement from the applicants, such a statement appears below.[1]

A copy of the priority document has been filed. It is in English. Therefore Bennet is not prior art.

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[1] For the record, however, undersigned notes that the interview in question was held between the hours of 3:00 p.m. and 4:00 p.m. on June 28, 2007, and the examiner indicated that as she had another interview at 4:00 p.m. that afternoon, she would not be able to immediately provide an Interview Summary. Moreover, there is no mailing date on the Interview Summary, and applicants have still not received a mailed copy of the Interview Summary, and therefore do not know the mailing date of such Interview Summary and therefore the date that the present statement would be due. Also, for the record, undersigned distinctly recalls requesting, at the conclusion of such interview at approximately 4:00 p.m. on June 28, 2007, that the examiner's "Interview Summary" not include the last paragraph requiring applicants to file a statement, in view of the fact that applicants had already submitted their arguments in the Reply previously filed, and undersigned on behalf of applicants further recalls the examiner's supervisor indicating in effect that this would not be a problem.

Dr. Larsson presented the background in ten minutes and emphasised IBMIR as the driving force for the present invention and underlined that Corline is in the process of starting clinical studies and that the patent is very important for Corline. Dr. Larsson also spent a few minutes on presenting the major differences between encapsulation and irreversible adsorption. The examiner's supervisor commented on IBMIR and at the end said he had been enlightened. The examiner said she had noticed the name Korsgren in a recent paper in Science.

Then followed a discussion for about forty minutes. The examiner advocated that the Corline Heparin Conjugate (CHC) should be classified as encapsulation. Dr. Larsson explained in some detail the chemical constitution of the CHC and underlined that CHC is a soluble macromolecule with no provisions for any cross-linking or polymerisation to occur after adsorption to the cell surface.

It was pointed out that the Advisory Action regarding Wagner reference is wrong in stating, "Additionally, if the cells are microencapsulated, they are first mixed with the anticoagulant material, thus anticipated the claims of the instant application." Wagner does not say so, and it was noted that such statement in the Advisory Action is an unwarranted extrapolation. Dr. Larsson pointed out that such statement makes no sense because if the cells were first mixed with an anticoagulant and then encapsulated, the anticoagulant could not

function. Dr. Larsson made a point of the fact that there is no disclosure in Wagner of first mixing the cells with heparin and then doing the encapsulation, and if it would have been disclosed, it would not have made sense.

There was a rather lengthy discussion of the Soon-Shiong (S-S) reference. The Examiner took the position that heparin is mentioned as a possible constituent according to the S-S reference and that this was enough to establish prior art. Dr. Larsson pointed out that heparin, if it were used despite the fact that none of the 32 examples contained any heparin, would be an integral part of the capsule and, hence, there is no disclosure in S-S of heparin being applied directly on to the cell surface.

Applicants argued that the islets in S-S are not contacted with heparin, even though heparin is mentioned as one of a large multitude of possible agents A, because Soon-Shiong uses a monomer A-X, and the presence of X, which must be in a major proportion, means that the contacting agent is something other than heparin. Applicants submitted that heparin could no longer be called heparin after being incorporated as part of A-X.

Dr. Larsson, who is an expert with regard to heparin, pointed out that heparin acts as a catalyst, and only a very small part of the heparin molecule acts as a catalyst to give heparin its ability to inhibit clotting; and consequently that it

is extremely unlikely that the polymerization of A-X, if heparin were A, would leave unimpaired the catalytic function of heparin to inhibit clotting.

The examiner's supervisor expressed his view that the Soon-Shiong method would result in islets being partially coated, along with free floating polymer. The supervisor invited Dr. Larsson to do some drawings to show the difference between encapsulation and irreversible adsorption. The supervisor said he had problems of understanding that the technique described in S-S would lead to spherical capsules and suggested that uncontrolled polymerisation would be more likely to occur. Dr. Larsson pointed out that this would make no sense because it would be contrary to the objective of Soon-Shiong.

In this regard, both Soon-Shiong and Wagner very clearly want to provide an impenetrable barrier by encapsulation, both attempting to provide improvements to the encapsulation technique which has been attempted for 20-30 years, whereas the present invention takes a fundamentally different approach. Dr. Larsson noted that encapsulated islets are only productive for a short period of time, because the capsule shells inhibit the establishment of capillaries, and eventually the encapsulated islets die. The capsule shells provide a barrier to blood in one direction and insulin in the other direction.

Soon-Shiong describes the problem of encapsulation with alginates as having poor stability due to the fact that

alginates are water-soluble. The S-S invention aims at making the capsules insoluble by cross-linking. Hence, Soon-Shiong still relies on the well-known technology of making microcapsules based on alginates but with the modification that he adds a monomer that can undergo free radical polymerisation so that the capsule becomes insoluble and, hence, acquires a better mechanical stability over a longer period of time.

As regards Bennet publication, applicants pointed out that it has a *prima facie* publication date after our priority date, and the burden is on the examiner to prove an earlier date. We filed a copy of the priority application with the last Reply and it is in English and is date stamped 05-Feb-99. Dr. Larsson pointed out that in any event Bennet does not disclose the present invention, but instead discloses administering heparin systemically.

Respectfully submitted,

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